

CLAIMS

1. A nucleic acid construct comprising (i) a nucleic acid sequence encoding a member of the lipocalin protein family, and (ii) a nucleic acid sequence encoding a peptide sequence of from 5 to 250 amino acid residues

5

2. A nucleic acid construct as claimed in claim 1, in which the lipocalin is selected from the group consisting of: ovine betalactoglobulin (BLG) (accession No. X12817), murine major urinary protein (MUP) (accession No. NM 031188) and rat α -2-urinary globulin (α -2u) (accession number M27434).

10

3. A nucleic acid construct as claimed in claim 1 or claim 2, in which peptide sequence is an epitope.

4. A nucleic acid construct as claimed in claim 3, in which the epitope is selected from the group consisting of EQKLISEEDL, GKPIPPLLGLDST, YPYDVPDYA, NVRFSTIVRRRA, KQMSDRRENDMSPS, SGNEVSRAVLLPQSC, SSSLSTNPAAVAATSANL, RSTLQHPDYLQEYST, VSTLLRWERFPGHRQA, KFFQQLVQCLTEFHAALGAYV, QEQCQEVWRKRVISAFKSP, and RLSDKTGPVAQEKs

20

5. A nucleic acid construct as claimed in any one of claims 1 to 4, in which the construct additionally comprises a promoter element upstream of the (i) a nucleic acid sequence encoding a member of the lipocalin protein family, and (ii) and nucleic acid sequence encoding a peptide sequence of from 5 to 250 amino acid residues.

25

6. A nucleic acid construct as claimed in claim 5, in which the promoter element may be selected from one of the following groups consisting of :

30

(i) c-myc, p21/WAF-1, MDM2, Gadd45, FasL, GAHSP40, TRAIL-R2/DR5, BTG2/PC3;

BEST AVAILABLE COPY

(ii) MnSOD, CuZnSOD, I κ B, ATF4, xanthine oxidase, COX2, iNOS, Ets-2, FasL/CD95L, γ GCS, ORP150.

(iii) Lrg-21, SOCS-2, SOCS-3, PAI-1, GBP28/adiponectin, α -1 acid glycoprotein, metallothioneine I, metallothioneine II, ATF3, IGFbp-3, VDGF and HIF1 α .

(iv) Gadd 34, GAHSP40, TRAIL-R2/DR5, c-fos, CHOP/Gadd153, APAF-1, Gadd45, BTG2/PC3, Peg3/Pw1, Siah1a, S29 ribosomal protein, FasL/CD95L, tissue transglutaminase, GRP78, Nur77/NGFI-B, CyclophilinD, p73 and Bak.

(v) a promoter from a xenobiotic metabolising cytochrome p450 enzymes from the 2A, 2B, 2C, 2D, 2E, 2S, 3A, 4A and 4B gene families.

(vi) a synthetic promoter sequence comprised of a minimal eukaryote consensus promoter operatively linked to one or more response elements selected from the group consisting of the aryl hydrocarbon (Ah)/Ah nuclear translocator (ARNT) receptor response element, the antioxidant response element (ARE), the xenobiotic response element (XRE).

7. A nucleic acid construct comprising a stress inducible promoter operatively isolated from a nucleic acid sequence encoding a member of the lipocalin protein family by a nucleotide sequence flanked by nucleic acid sequences recognised by a site specific recombinase, or by insertion such that it is inverted with respect to the transcription unit encoding a member of the lipocalin protein family, in which the construct additionally comprises a nucleic acid sequence comprising a tissue specific promoter operatively linked to a gene encoding the coding sequence for the site specific recombinase.

8. A nucleic acid construct as claimed in claim 7, in which the site specific recombinase sequences are two *loxP* sites of bacteriophage P1.

9. A host cell transfected with a nucleic acid construct according to any one of claims 1 to 8.
- 5 10. A transgenic non-human animal in which the cells of the non-human animal express the protein encoded by the nucleic acid construct according to any one of claims 1 to 8.
- 10 11. A transgenic non-human animal as claimed in claim 10, in which the non-human animal is a mammal
12. A transgenic non-human mammal as claimed in claim 11, in which the mammal is a mouse
- 15 13. The use of a nucleic acid construct according to any one of claims 1 to 8 for the detection of a gene activation event resulting from a change in altered metabolic status in a cell *in vitro* or *in vivo*.
- 20 14. A use as claimed in claim 13, in which the gene activation event is the induction of toxicological stress, metabolic changes, or disease, including a disease state that is the result of viral, bacterial, fungal or parasitic infection.
- 25 15. The use of a nucleic acid construct comprising a nucleic acid sequence encoding a member of the lipocalin protein family, wherein said lipocalin protein is heterologous to the cell in which it is expressed, for the detection of a gene activation event resulting from a change in altered metabolic status in a cell *in vitro* or *in vivo*.
- 30 16. A use as claimed in claim 15, in which the gene activation event is induction of toxicological stress, metabolic changes, or disease, including a disease that is the result of viral, bacterial, fungal or parasitic infection.

BEST AVAILABLE COPY

17. A method of detecting a gene activation event in a cell *in vitro* or *in vivo*, comprising assaying a host cell stably transfected with a nucleic acid construct in accordance with any one of claims 1 to 8, or a transgenic non-human animal according to any one of claims 10 to 12, in which the cell or animal is subjected to a gene
5 activation event that is signalled by expression of a peptide tagged lipocalin reporter gene.

18. A method of detecting a gene activation event in a cell *in vitro* or *in vivo*, comprising assaying a host cell stably transfected with a nucleic acid construct
10 comprising a nucleic acid sequence encoding a member of the lipocalin protein family, wherein said lipocalin protein is heterologous to the cell in which it is expressed, or a transgenic non-human animal whose cells express such a construct, in which the cell or animal is subjected to a gene activation event that is signalled by expression of a peptide tagged lipocalin reporter gene.

19. A method of screening for, or monitoring of toxicologically induced stress in a cell or a cell line or a non-human animal, comprising the use of a cell, cell line or non human animal which has been transfected with or carries a nucleic acid construct according to any one of claims 1 to 8.

20. A method for screening and characterising viral, bacterial, fungal, and parasitic infection comprising the use of a cell, cell line or non human animal which has been transfected with or carries a nucleic acid construct according to any one of claims 1 to 8.

21. A method for screening for cancer, inflammatory disease, cardiovascular disease, metabolic disease, neurological disease and disease with a genetic basis comprising the use of a cell, cell line or non human animal which has been transfected
25 with or carries a nucleic acid construct according to any one of claims 1 to 8.